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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,382	09/09/2004	Jian Luo	MGC020325	6441

7590 01/06/2009

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EXAMINER	
DICKINSON, PAUL W	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
01/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,382	LUO ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-11* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/3/2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Claim Rejections - 35 USC § 102 and 103

The rejection of claims 1-3, 7, and 9-10 under 35 U.S.C. 102(b) as being anticipated by Paterniti et al (WO 9805331) is maintained. The rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Paterniti et al (WO 9805331) is maintained. The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Barelli et al (US 5922796) in view of Ko et al (Current Therapeutic Research, 1995) is maintained.

Applicant argues that the composition disclosed by Paterniti et al comprises a PPARgamma agonist. By contrast, the instant claims now recite "consisting of" which excludes the presence of any non-recited elements. Claim 8 has been amended to delete the term "about" and the claim should now be distinguishable over Barelli et al in view of Ko et al.

Applicant's arguments have been fully considered but are not found persuasive.

Regarding Paterniti et al, the Examiner agrees that instant claim 1 now recites "consisting of" which excludes the presence of any non-recited elements. However, one

recited element in the composition is "one or more pharmaceutically acceptable ingredients". A PPARgamma agonist is a pharmaceutically acceptable ingredient.

Regarding the rejection of claim 8, the Examiner maintains that it would be obvious to add the glucose-lowering agent and the lipid-improving agent at the same time to treat diabetes mellitus, as both of these compounds are known in the art to treat diabetes mellitus.

Interview Summary

Regarding the interview summary dated 3/28/2008, Applicant argues against a rejection under 35 U.S.C. 103(a) based on Weintraub et al (Atherosclerosis, 1998) in view of FR 2796940. Applicant is clear that this is assuming that the Examiner intends to make this rejection. As a courtesy to the Applicant, the Examiner cited these references in the interview summary as references that alone (not in combination), may serve as prior art against a composition consisting of metformin, gemfibrozil, and a pharmaceutically acceptable ingredient. A rejection under 35 U.S.C. 103(a) relying on Weintraub et al in view of FR 2796940 is not of record (or made in this action), and the Examiner will not respond to Applicant's arguments at this time.

New Grounds of Rejection

Claim Rejections - 35 USC § 112 - Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the recited conditions, does not reasonably provide enablement for preventing the recited conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to prevent the recited conditions commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

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[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to preventing diseases, disorders selected from the group consisting of diabetes mellitus, hyperglycemia, imparied glucose-tolerance, insulin resistant syndrome, obesity, pancreatitis and other disorders where absnormally in plasma glucose levels or glucose metabolism is a component. The relative skill of those in the art is high, that of an MD or PhD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites http://www.webmd.com/diet/what-is-obesity (accessed 1/3/2009) which teaches that the causes of obesity are multifaceted, and factors such as age, gender, genetics, environemtnal factors, physical activity, psychological factors, illness, and medication all play a roll.

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term "prevention", the examiner will adopt the broadest reasonable interpretation for same. Webster's Ninth New Collegiate Dictionary defines "prevention" as "to keep from happening or existing", i.e., to completely eradicate. The claims are thus very broad insofar as they recite the "prevention" of the recited conditions,, i.e., the complete eradication of same. While such "prevention" might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the "real world" in which patients live; recurrence is always a risk.]

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for preventing the conditions recited in claim 9. No reasonably specific guidance is provided concerning useful therapeutic protocols for preventing these conditions, other than treating these conditions. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to prevent the recited conditions as inferred by the claim and contemplated by the specification. Accordingly, the instant

claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

5. Suggested alternative language

Since the term "treating" is inclusive of various administrative timing schemes and thus provides adequate coverage for all reasonably successful therapies (prophylactic or active), the examiner recommends deleting the term "preventing" and simply reciting "treatment" only instead.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weintraub et al (Atherosclerosis, 1998; document already in record). Weintraub et al discloses that gemfibrozil and metformin are shown to be beneficial for the clearance of PPLp in hypertriglyceridemic patients (see abstract; Discussion). Gemfibrozil was administered at 1200 mg/day and metformin was administered separately at 1700 mg/day (see Table 1). Weintraub et al fails to disclose a pharmaceutical composition consisting of (1) metformin and (2) gemfibrozil in combination with one or more pharmaceutically acceptable ingredients.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to prepare a formulation comprising gemfibrozil and metformin in combination with a pharmaceutical excipient. In this way, dosage form that clears PPLp in hypertriglyceridemic patients will be obtained. It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072

(CCPA 1980). It would be further obvious to find Applicant's metformin to gemfibrozil weight ratio ranges of 1:0.1 to 1:10 and 1:0.5 to 1:2, through routine experimentation, to afford a more effective dosage form for clearning PPLp in hypertriglyceridemic patients. Weintraub et al discloses administering 1700 mg/day of metformin and 1200 mg/day of gemfibrozil. If these two dosage forms were combined together, the metformin to gemfibrozil weight ratio would be 1700:1200, or 1:0.71. This weight ratio is encompassed by the instantly claimed ranges, and thus it would be obvious to find these ranges through routine experimentation. See MPEP § 2144.05, II.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Paterniti et al (WO 9805331; document already in record). Paterniti et al discloses a pharmaceutical composition comprising metformin, a PPARalpha agonist, and a pharmaceutically acceptable carrier (see page 13, lines 19-29). Metformin is added in a pharmaceutically effective amount (see ibid). Paterniti et al discloses gemfibrozil as a preferred PPARalpha agonist (see page 8 line 28 to page 9 line 1). Paterniti et al further discloses that gemfibrozil may be administered at 50 mg/kg/day (see page 14, lines 16-20). Paterniti et al discloses that it is well within the capability of those skilled in the art, especially in light of the detailed disclosure, to determine effective amounts (page 39, lines 14-17) and that the exact formulation can be chosen by the individual physician in view of the patient's condition (see page 37, lines 6-8). Paterniti et al fails to disclose a composition wherein the weight ratio of metformin and gemfibrozil ranges from 1:0.5 to 1:2.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to optimize the ratio of metformin to gemfibrozil, through routine experimentation, to afford a pharmaceutical composition for the treatment of Type 2 diabetes. In this way, one would find the presently claimed weight ratio range of 1:0.5 to 1:2. The rationale for this is that Paterniti et al discloses adding 50 mg/kg/day of gemfibrozil, and further discloses adding a pharmaceutically effective amount of metformin. It would be obvious to optimize the relative ratio of each, as taught by Paterniti et al, to determine amounts most effective for the most effective treatment against Type 2 diabetes (see page 39, lines 14-17). See MPEP § 2144.05, II.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

January 3, 2009